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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1654	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,975	C. TAO ET AL.	
	Examiner	Art Unit	
	Michele C. Flood	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *31 July 2003* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *9-13,15,19-21 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,14,16-18,22,23 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Acknowledgment is made of Applicant's withdrawal of Claims 24-31. Applicant's election with traverse of the species of an oral dosage of a high molecular weight, lipophilic, bioactive agent, comprising an antioxidant, a lipid matrix, and resveratrol, in Paper No. 11 is acknowledged. The traversal is on the ground that there is no undue burden for the examiner to search and examine additional species comprising other distinct ingredients of Claims 5, 8, 9 and 18 because the species are encompassed with generic Claim 1. Thus, Applicant concludes that search for matter within Claim 1 would necessarily require a search of the instantly claimed invention.

This is not found persuasive because each of the additional species comprising the other distinct ingredients of Claims 5, 8, 9 and 18 are separate and distinct. Thus, they require materially different searches; a search of the art for one ingredient would not necessarily encompass all of the ingredients. Additional search terms would be required for a thorough search of each of the claimed ingredients, thus resulting in a larger more burdensome search for the examiner.

Hence, the search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further a reference that would anticipate the invention of one species would not necessarily anticipate or even make obvious another species. Finally, the consideration for patentability is different in each case. Thus, it would be an undue burden to examine all of the above inventions in one application.

The requirement is still deemed proper and is therefore made **FINAL**.

Acknowledgment is made of Applicant's listing of Claims 1-8, 14-26, and 32-33, as reading on the elected species. However, upon further review of the elected invention, the Office deems that Claims 1-8, 14, 16-18, 22, 23 and 32 read on the elected invention, wherein Applicant has elected the species resveratrol.

Claims are under 1-8, 14, 16-18, 22, 23 and 32 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 7, 15, 16, 18 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6, line 1, recites the limitation "wherein the lipid matrix". There is not clear antecedent basis for the limitation in the claim. Applicant may overcome the rejection by adding triglyceride, after "the".

The metes and bounds of Claim 16 are rendered uncertain by the phrase "wherein the polyphenol comprises resveratrol" because it is unclear as to the subject matter Applicant intends to direct the invention. For instance, it is unclear as to how a polyphenol comprises resveratrol since resveratrol is a polyphenol. Does Applicant intend to direct the invention to a composition wherein the polyphenol is resveratrol? The lack of clarity renders the claim vague and indefinite.

The metes and bounds of Claim 15 are rendered vague and indefinite by the phrase "wherein the polyphenol comprises *Polygonum cuspidatum* extract" because it is unclear as to the subject matter Applicant intends to direct the invention. For instance, while it is known in the art that an extract of *Polygonum cuspidatum* comprises resveratrol, it is also known that the recited plant extract also comprises other chemical compounds. Thus, it would appear that Applicant claims an invention beyond the scope of the instantly claimed invention, namely the polyphenol resveratrol. Also, it would appear that Applicant intends to direct the invention to wherein the polyphenol comprises resveratrol is derived from an extract of *Polygonum cuspidatum*. However, as drafted, Claim 15 lacks clarity.

With regard to Claim 18, line 3, there is an apparent misspelling. Applicant may overcome the rejection by replacing "rosmarrinic acid" with rosmarinic acid.

Claim 22, as drafted, in its entirety, is rendered vague and indefinite because the instantly claimed percent amounts of the recited ingredients comprising the claimed ingredients are not related to a specified mass amount. For instance, does the claimed percent amount refer to the total weight of the composition or to the total volume of the composition? The lack of clarity renders the metes and bounds of the claim uncertain.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8, 14 and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Chopra (N) and Claims 1-8, 14 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Chopra (A).

Applicant claims an oral dosage composition of a high molecular weight, lipophilic, bioactive agent, comprising: a biologically effective amount of the bioactive agent; a lipid matrix in which the bioactive agent is suspended; and a sufficient amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered. Applicant further claims the composition of claim 1, wherein the lipid matrix comprises a triglyceride matrix that is a liquid at body temperature. Applicant further claims the composition of claim 2, wherein the triglyceride matrix comprises a soybean lipid matrix. Applicant further claims the composition of claim 1, wherein the bioactive agent has a molecular weight of at least 200. Applicant further claims the composition of claim 4, wherein the bioactive agent comprises one or more of an ingredient(s) in a recited Markush group. Applicant further

claims the composition of claim 3, wherein the lipid matrix comprises a mixture of refined soybean oil; mono-, di- and triglycerides, and polyglycerol oleate and/or polyglycerol dioleate. Applicant further claims the composition of claim 6, wherein the di- and triglycerides are glycerides having side chains with 16 to 18 carbons. Applicant further claims the composition of claim 1 wherein the composition of claim 1 wherein the polyphenol comprises resveratrol; wherein the bioactive agent comprises a Coenzyme Q in either its reduced form (ubiquinone) or oxidized form (ubiquinol). Applicant further claims the composition of claim 8, wherein the polyphenol comprises resveratrol. Applicant further claims the composition of claim 1, comprising about 8-10% bioactive agent, less than about 1% polyphenol, and about 85-90% lipid matrix.

Chopra (A, referred herein for convenience as both A and N contain the same subject matter) teaches a composition comprising a biologically effective amount of a high molecular weight, lipophilic, bioactive agent, *i.e.*, Coenzyme Q or Coenzyme Q in its reduced form (ubiquinone) in an amount ranging from 0.5%-15% or 1% to about 10% (*see* Column 1, line 64 to Column 2, line 4); a lipid matrix in which the bioactive agent is suspended, *i.e.*, vegetable oil or a triglyceride or a phospholipid derived from soy or egg (*see* Column 2, lines 7-14; Column 4, line 21 to Column 5, line 31; and, Column 6, line 64 to Column 7, line 41), wherein the amount of triglyceride ranged from about 0.1% to about 35% by weight of the composition and wherein the amount of phospholipid ranged from about 0% to about 25%, preferably about 1.0% to about 15% by weight of the composition; and a sufficient amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered, *i.e.*,

resveratrol, grape seed extract, flavonoids, *etc.* (*see* Column 6, line 42 to Column 7, line 8), wherein the amount of the polyphenol ranged from 0.1% to about 20%, more preferably about 0.01% to about 25% by weight of the composition (*see* Column 8, lines 1-5). *See* Claims (especially, Claims 10-15, 18, 20-3, 26-28, and 30-32).

Chopra does not expressly teach that the polyphenol comprising his composition improves gastrointestinal absorption of the bioactive agent when the dosage form is orally administered. However, the ingredients comprising the composition taught by Chopra are one and the same as the ingredients comprising the composition claimed by Applicant, and the amounts of the ingredients thereof are one and the same as claimed by Applicant. Therefore, the functional effect of the polyphenol comprising the composition taught by Chopra is inherent to the composition taught by Chopra.

Each of the references of Chopra (A and N) anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 14, 16-18, 22, 23 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chopra (A or N) in view of Chopra (A or N).

Applicant's claimed invention of Claims 1-8, 14 and 22 was set forth above. Applicant further claims the composition of claim 1, further comprising an antioxidant other than the polyphenol or bioactive agent. Applicant further claims the composition of claim 17, wherein the antioxidant comprises one or more of Vitamin A, Vitamin E (tocopherol), Vitamin K, copper, zinc, iron, selenium, beta-carotene, eriodicytol, carnosic acid, carnosol, rosmarinic acid, caffeic acid, coumaric acid, cinnamic acid, Coenzyme Q, Probucol, astaxanthin, lycopene, alpha-lipoate, and urate. Applicant further claims the composition of claim 1, further comprising 2-3% of an antioxidant other than the bioactive agent and polyphenol. Applicant further claims the composition of claim 18, wherein the antioxidant comprises a pharmaceutically acceptable salt or ester of the antioxidant.

The teachings of Chopra are set forth above. Chopra does not expressly teach a composition further comprising an antioxidant other than the bioactive agent and polyphenol, wherein the composition further comprises 2-3% of an antioxidant other than the bioactive agent and polyphenol, and wherein the antioxidant comprises a pharmaceutically acceptable salt or ester of the antioxidant. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add the instantly claimed ingredients in the instantly claimed amounts to the composition taught by Chopra to provide the claimed composition because, in Column 9, lines 20-36, Chopra teaches adding ubiquinone to a premixed solution of triglyceride (and optionally, vitamin E or a vitamin E ester), and adding additional bioactive agents. At the time the invention was made, one of ordinary skill in the art would have been

motivated and one would have had a reasonable expectation of success to add an amount of an additional antioxidant other than the bioactive agent and the polyphenol comprising the composition taught by Chopra (such as, those ingredients recited in the Markush of Claim 18) to provide the claimed invention because Chopra teaches that the active components of his composition can be mixed with other active materials, which do not adversely impair their [therapeutic] action, *e.g.*, Vitamin E (tocopherol) and esters thereof, alpha-lipoic acid, *etc.*, in Column 9, lines 54-63.

With regard to the limitation of Claim 23, wherein Applicant claims a composition of claim 1 further comprising 2-3% of an antioxidant other than the bioactive agent and polyphenol, it also would have been obvious to one of ordinary skill in the art to optimize the referenced composition by adjusting the amount of antioxidant ingredients taught by Chopra to provide the claimed composition because Chopra suggests that any amount of any other active ingredient can be added in the making of his composition, as long as the active ingredient does not unfavorably affect the effect of the other components comprising the referenced composition. At the time the invention was made, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to optimize the Chopra' composition by adjusting the amount of antioxidant comprising the composition taught by Chopra to the instantly claimed percentage amount to provide the claimed invention because Chopra teaches, in Column 7, lines 8-48 and Column 9, lines 20-63, the amounts of additional antioxidants which can be used in the making of the referenced composition and teaches that such ingredients provide therapeutic beneficial effects when administered

to patients for various treatments. Thus, the effective varying of the amounts of the antioxidants taught by Chopra would have been no more than a routine matter of optimization for one of ordinary skill in the art at the time the invention was made.

According, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is (703) 308-9432. The examiner can normally be reached on Monday through Friday from 7:15 am to 3:45 pm. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196 or the Supervisory Patent Examiner, Brenda Brumback whose telephone number is (703) 306-3220.

MICHELE FLOOD
PATENT EXAMINER

Michele C. Flood

MCF

October 14, 2003